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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	08/870,762	DUFT ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on th cov r sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosur Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *062702*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendments filed 03/14/06, 12/06/05, 09/30/05 and 12/02/02 in response to the non-final Office Action mailed 05/30/02.

Status of Claims

2) New claims 7-16 have been added via the amendment filed 12/02/02.

Claim 3 has been amended via the amendment filed 09/30/05.

Claim 1 was amended via the amendment filed 09/30/05 by deleting the previous limitation 'and a pharmaceutically acceptable carrier', but the deletion was not indicated by a strikethrough. The status identifier of the claim was not indicated as '(Currently amended)'. The amendment submitted 03/14/06 presents claim 1 in its previous form wherein the limitation 'and a pharmaceutically acceptable carrier' is retained as a part of the claim.

Claim 7 has been amended via the amendment filed 03/14/06.

Claims 1-16 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Information Disclosure Statement

5) Acknowledgment is made of Applicants' Information Disclosure Statement filed 06/27/02. The information referred to therein has been considered, except the documents, which have already been considered or cited on a PTO-892, and a signed copy is attached to this Office Action.

Declaration under 37 C.F.R 1.131

6) Acknowledgment is made of Applicants' declaration under 37 CFR 1.131 filed 12/02/02 antedating the reference of Thompson *et al.* (May, 1997).

Substitute Specification

7) Acknowledgment is made of Applicants' most recent substitute specification filed 09/30/05.

Substitute Sequence Listing

8) Acknowledgment is made of Applicants' most recent substitute Sequence Listing filed 03/14/06, which has been entered.

Specification/Claims

9) 37 CFR 1.75(d)(1) provides, in part, that 'the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description.'

Claim 33 includes the limitation 'active anti-obesity agent' which lacks clear support or antecedent basis in the specification.

Specification

10) The instant specification is objected to for the following reason(s):

(a) The paragraphs added via the amendment filed 12/02/02 to the specification following Example 8 (see Examples 9-22 of the substitute specification), including the paragraph identified below constitute new matter (see last paragraph on page 32 of the substitute specification):

> To assist in understanding the present invention, the following further Examples A-N are included and describe the results of a series of experiments therein. The following examples relating to this invention should not, of course, be construed as specifically limiting the invention. Such variations of the invention, now known or later developed, which would be within the purview of one skilled in the art are considered to fall within the scope of the present invention as hereinafter claimed.

To incorporate material by reference, the host document/application must identify with

detailed particularity what specific material it incorporates and clearly indicate where the material is found in the various documents. See *Advanced Display Systems, Inc. v. State Univ.*, 54 USPQ2d 1673 (Fed. Cir. 2000) citing *In re Seversky*, 177 USPQ 144, 146 (CCPA 1973). In the instant application, the only material that was particularly identified as being incorporated was the '[u]seful amylin agonist analogues' identified in an International Application, WPI Acc. No. 93-18488/22. See top of page 10 of the substitute specification. The above-identified paragraph describing the 'variations' of the invention and the methods of 'Preparation of' or synthesis of various amylin agonist analogues as recited in the newly added Examples of 9-22, were not materials specifically identified as being incorporated, in the instant specification.

Objection(s) Withdrawn

11) The objection to the specification made in paragraph 5(a) of the Office Action mailed 05/30/02 is withdrawn.

12) The objection to the specification made in paragraph 5(b) of the Office Action mailed 05/30/02 is withdrawn in light of Applicants' explanation.

13) The objection to the specification made in paragraph 5(c) of the Office Action mailed 05/30/02 is withdrawn in light of Applicants' amendment to the specification.

Rejection(s) Withdrawn

14) The rejection of claims 5 and 6 made in paragraph 13 of the Office Action mailed 11/13/00 (paper no. 21) under 35 U.S.C § 103(a) as being unpatentable over Arnelo *et al.* (Arnelo *et al. Am. J. Physiol.* 271: 6 pt 2: R1654-R1659, December 1996) (Arnelo *et al.* I), or Arnelo *et al.* (*Scand. J. Gastroenterol.* 31: 83-89, January 1996) (Arnelo *et al.* II) as applied to claims 4 and 1, and further in view of Bennett *et al.* (US 5,955,443) and maintained in paragraph 8 of the Office Action mailed 12/18/01 (paper no. 28) and paragraph 7 of the Office Action mailed 05/30/02, is withdrawn in light of the new rejection(s) set forth below.

15) The rejection of claims 1-6 made in paragraph 14 of the Office Action mailed 11/13/00 (paper no. 21) under 35 U.S.C § 103(a) as being unpatentable over Kolterman *et al.* (WO 96/40220, already of record) (Kolterman *et al.*, II) in view of Meglasson (US 5,134,164) and

maintained in paragraph 9 of the Office Action mailed 12/18/01 (paper no. 28) and paragraph 8 of the Office Action mailed 05/30/02, is withdrawn in light of the modified rejection made below.

16) The rejection of claims 1-6 made in paragraph 11 of the Office Action mailed 05/30/02 under the judicially created doctrine of double patenting over the claims 1-25) of the U.S. Patent US 6,114,304 (Kolterman *et al.*) in view of Weintraub *et al.* (*Nutrition Rev.* 49: 237-249, 1989) and Robert *et al.* (WO 91/16917), is withdrawn.

17) The rejection of claims 1-6 made in paragraph 16 of the Office Action mailed 05/30/02 under 35 U.S.C § 102(a) as being anticipated by Thompson *et al.* (*Diabetes* 46: Suppl. 1, page 30A, 0116, 02 May 1997) (Thompson *et al.*, May, 1997), is withdrawn in light of Applicants' submission of a Declaration under 37 CFR 1.131 antedating the reference.

18) The rejection of claims 1-3 made in paragraph 17 of the Office Action mailed 05/30/02 under 35 U.S.C § 102(b) as being anticipated by MacDonald *et al.* (*Diabetologia* 38: Suppl. 1, A118, August 1995, Applicants' IDS) as evidenced by Robert *et al.* (WO 91/16917), is withdrawn in light of the new rejections set forth below.

19) The rejection of claims 1-6 made in paragraph 18 of the Office Action mailed 05/30/02 under 35 U.S.C § 102(a) as being anticipated by Thompson *et al.* (*Diabetes* 46: 632-636, April 1997, already of record) (Thompson *et al.*, April, 1997) as evidenced by Guthrie *et al.* (US 4,443,619), is withdrawn in light of Applicants' submission of a Declaration under 37 CFR 1.131 antedating the reference of Thompson *et al.* (April, 1997).

20) The rejection of claims 1-6 made in paragraph 19 of the Office Action mailed 05/30/02 under 35 U.S.C. § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) in light of *The Random House Dictionary* (Ed. Flexner *et al.*, Random House, page 32, New York, 1984), is withdrawn in light of the modified rejection made below.

21) The rejection of claims 1-6 made in paragraph 20 of the Office Action mailed 05/30/02 under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (WO 95/07098), is withdrawn in light of the new rejections set forth below.

22) The rejection of claims 1-6 made in paragraph 21 of the Office Action mailed 05/30/02 under 35 U.S.C. § 103(a) as being unpatentable over Kolterman *et al.* (*Diabetologia* 39: 492-499, April 1996, already of record) (Kolterman *et al.*, 1996) in view of Robert *et al.* (WO 91/16917), is withdrawn in light of the modified rejection set forth below.

23) The rejection of claims 1-6 made in paragraph 22 of the Office Action mailed 05/30/02 under 35 U.S.C. § 103(a) as being unpatentable over Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) or Kolterman *et al.* (WO 95/07098) ('098) in view of Frishman *et al.* (*In*: *Cardiovascular Pharmacotherapeutics.* (Eds) Frishman WH *et al.* McGraw-Hill Health Professions Division, New York, Chapter 48, pages 1093-1114, February 1997), or Weintraub *et al.* (*Nutrition Rev.* 49: 237-249, 1989), is withdrawn in light of the modified rejection set forth below.

24) The rejection of claims 1-3 made in paragraph 23 of the Office Action mailed 05/30/02 under 35 U.S.C § 103(a) as being unpatentable over Kong *et al.* (*Diabetologia* 40: 82-88, January 1997, Applicants' IDS) (Kong *et al.*, 1997), or MacDonald *et al.* (*Diabetologia* 38: Suppl. 1, A118, August 1995, Applicants' IDS) in view of Robert *et al.* (WO 91/16917) and Jonderko *et al.* (*Aliment. Pharmacol. Ther.* 5: 413-418, 1991) (Jonderko *et al.*, 1991) and Frishman *et al.* (*In*: *Cardiovascular Pharmacotherapeutics.* (Eds) Frishman WH *et al.* McGraw-Hill Health Professions Division, New York, Chapter 48, pages 1093-1114, February 1997) or Morley *et al.* (*Pharmacol. Biochem. Behav.* 44: 577-580, 1993) (Morley *et al.*, 1993), is withdrawn.

25) The rejection of claims 1-6 made in paragraph 24 of the Office Action mailed 05/30/02 under 35 U.S.C § 103(a) as being unpatentable over Kolterman *et al.* (WO 95/07098) ('098) or Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) in view of Morley *et al.* (*Pharmacol. Biochem. Behav.* 44: 577-580, 1993) (Morley *et al.*, 1993) and Jonderko *et al.* (*Aliment. Pharmacol. Ther.* 5: 413-418, 1991) (Jonderko *et al.*, 1991), is withdrawn in light of the modified rejection set forth below.

26) The rejection of claims 1-6 made in paragraph 25 of the Office Action mailed 05/30/02 under 35 U.S.C § 103(a) as being unpatentable over Kolterman *et al.* (WO 95/07098) (Kolterman

et al., '098) or Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996) in view of Frishman *et al.* [*In*: *Cardiovascular Pharmacotherapeutics*. (Eds) Frishman WH *et al.* McGraw-Hill Health Professions Division, New York, Chapter 48, pages 1093-1114, February 1997] and Jonderko *et al.* (*Israel J. Med. Sci.* 25: 20-24, 1989) (Jonderko *et al.*, 1989) or Guthrie *et al.* (US 4,443,619), is withdrawn in light of the modified rejection set forth below.

Rejection(s) Maintained

27) The provisional rejection of claims 1-6 made in paragraph 10 of the Office Action mailed 11/13/00 (paper no. 21) under the judicially created doctrine of double patenting over the claims of the pending application, SN 09/445,517, and maintained in paragraph 9 of the Office Action mailed 05/30/02, is still maintained for reasons set forth therein. Applicants state that a terminal disclaimer will be filed upon withdrawal of all other outstanding rejections.

28) The rejection of claims 1-6 made in paragraph 12 of the Office Action mailed 05/30/02 under 35 U.S.C § 112, first paragraph, as containing new matter, is maintained for reasons set forth therein and herebelow.

New claims 8-13 are now included in this rejection.

Applicants present the following arguments: (a) The present application states that the invention is directed to 'novel methods for treating or preventing obesity' and describes methods to decrease body weight. (b) The methods involve administration of an amylin or an amylin agonist, and the application at page 13 goes on to state that 'treating or preventing' obesity includes 'combating' or 'eliminating' the disease. (c) The *American Heritage Dictionary* of the English Language defines the prefix 'anti-' to mean 'opposing' or 'counteracting'. (d) The amylins and amylin agonists administered in the described and claimed methods for treatment of obesity that decrease weight may thus be referred to as 'anti-obesity agents'. (e) The abstract refers to amylin or amylin agonist of the invention as an 'obesity relief agent'.

Applicants' arguments have been carefully considered, but are not persuasive. The Office agrees with the Applicants that the abstract provides descriptive support for the limitation 'obesity relief agent'. However, the limitation in the claim that lacks descriptive support is not 'obesity

relief agent', but 'anti-obesity agent'. Contrary to Applicants' assertion, page 13 of the specification does not mention of 'treating or preventing' obesity, or 'combating' or 'eliminating' the disease. See page 13 of the amended or substitute specification filed 09/30/05. The specification as originally filed did not include the term 'anti-obesity agent', or 'an effective amount of a composition comprising an anti-obesity agent'. How a *Dictionary* defines a term that was never a part of the originally filed specification is irrelevant. The support for a limitation must come from Applicants' specification as filed, not from a *Dictionary*. Example 1 of the specification and the art at the time indicate that the amylin agonist, pramlintide, is an anti-diabetic agent. The specification as originally filed appear to suggest that pramlintide used for 'combating' or 'eliminating' the disease is described in the instant specification as an 'obesity relief agent' (see line 9 on page 9 of the substitute specification filed 09/30/05). The rejection stands.

29) The rejection of claim 1 made in paragraph 14(a) of the Office Action mailed 05/30/02 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for reasons set forth therein and herebelow.

New claims 7 and 16 are now added to this rejection since both of these new claims include the limitation 'effective amount'.

Applicants cite case law and acknowledge that under the law of indefiniteness, the Office's rejection is appropriate. See lines 16 and 17 on page 99 of Applicants' response filed 12/02/02. Applicants present the following arguments. (a) If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, section 112 demands no more. (b) Given the teachings of the specification, one of ordinary skill in the art can readily understand the metes and bounds of the claimed invention. The claim reference to an 'effective amount' is plainly a reference to an amount effective to treat or prevent obesity. (c) In *In re Watson*, 186 USPQ2d 1869 (Fed. Cir. 2001), the Court reversed the rejection based on alleged indefiniteness of 'effective amount' as used in the phrase 'an effective amount of a germicide suitable for use in oral hygiene' and held that the very term 'germicide' used in the claim indicates that germicidal action is the effect sought to be produced and that those skilled in the art will be

able to determine from the disclosure, including the examples, what an effective amount of germicide is. (d) The PTO has provided no evidence that one skilled in the art would not understand the term 'effective' as used in the specification.

Applicants' arguments have been carefully considered, but are not persuasive. Contrary to Applicants' assertion, the instant specification does not reasonably apprise those skilled in the art the scope of the invention. For example, the human subjects used in Example 1 of the specification are patients with type II diabetes mellitus. For example, the amount of the amylin agonist, pramlintide, administered to type II diabetic patients in Example 1 of the instant specification is 30 micrograms QID, 60 micrograms TID, or 60 micrograms QID. A review of the prior art on the therapeutic use of pramlintide indicates that an amount of 30 micrograms QID, 60 micrograms TID, or 60 micrograms QID of pramlintide is administered subcutaneously to type II diabetic patients. See page 21, lines 15-27 of Kolterman *et al.* (WO 96/40220). Therefore, 30 micrograms QID, 60 micrograms TID, or 60 micrograms QID of pramlintide administered to a diabetic patient as in Example I of the instant specification qualify as amounts 'effective to treat diabetes mellitus', in the absence of a clear description to the contrary. Thus, contrary to Applicants' assertion, from the teachings of the instant specification, one of ordinary skill in the art cannot readily understand the metes and bounds of the limitation: 'effective amount'. The instant specification does not reasonably apprise those skilled in the art of the precise scope of the invention. The rejection stands.

30) The rejection of dependent claims 2-6 made in paragraph 14(b) of the Office Action mailed 05/30/02 under 35 U.S.C § 112, second paragraph, as being indefinite, is maintained for reasons set forth in and *supra*.

New dependent claims 8-13 and 15 are now added to this rejection.

Response to Applicants' Arguments on Art Rejection(s)

31) Applicants' arguments with regard to the prior art rejections are moot in light of Applicants' amendments to the claims and/or the withdrawal of the rejections. Those of Applicants' arguments that are pertinent to the new/modified art rejection(s) set forth below are addressed herebelow.

(A) Kolterman *et al.* (1996)

Applicants cite case law and submit the following arguments: (a) Kolterman *et al.* (1996) did not make the conclusions that are made by the Office. (b) The Office has not discharged the burden of establishing that the allegedly inherent feature or features necessarily flow from the teachings of Kolterman *et al.* (April, 1996). (c) Kolterman *et al.* (April, 1996) related to normally thin type 1 diabetics 'is silent about body weight'. (c) Kolterman *et al.* (April, 1996) say 'nothing about body weight, weight reduction', weight control, treatment of obesity, or treatment of obese individuals – let alone, as hypothesized by the Office, improving the bodily appearance of individuals given pramlintide. (d) The paper concludes with no reference to weight or obesity, but only with the statement that the observations from the study will be extended in future studies to evaluate the extent to which amylin replacement can improve glucose control throughout the entire 24 h period. (e) As a matter of law this cannot establish inherency of the claimed methods of treating obesity, which can only be demonstrated by a showing that the methods are the inherent, inevitable result of the practice of another method. (f) Inherency may not be established by probabilities or possibilities. (g) In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.

Applicants' arguments have been carefully considered, but are not persuasive. As explained under the modified art rejection set forth below Kolterman *et al.* (April, 1996), published more than a year before the filing date of the instant application, did indeed teach a method of reducing body weight in diabetic human subjects by subcutaneous administration of 30 micrograms of pramlintide for fourteen days (see Table 1 in particular). At the end of four weeks of subcutaneously administered pramlintide treatment, Kolterman *et al.* (April, 1996) clearly demonstrated a detectable weight loss in the diabetic patients as expressly depicted in Table 1. In this regard, it is noted that Applicants themselves have acknowledged that a decrease in body weight is detectable by two weeks of treatment. See last paragraph on page 10 of Applicants' response dated December 2002 filed in the related co-pending application 09/445,517.

Contrary to Applicants' assertion, Kolterman *et al.* (April, 1996) do not refer to their type

I diabetic patients as 'normally thin' type 1 diabetics. It should be noted that a 70 kg patient is not excluded from the scope of the instant invention, but is expressly included. For example, the recited amount range of 'about 0.01 to about 5 mg/day' of amylin agonist, for example, pramlintide, is specifically "for a 70 kg patient". See lines 4-8 of page 23 of the substitute specification; and paragraph bridging pages 23; and 24 and lines 3-7 on page 24 of Applicants' response filed December 2002. This is important because the mean body weight $\pm$ SEM of Kolterman's (1996) diabetic placebo population was 74.5 $\pm$ 2.4 kg, whereas the mean body weight of the 15 diabetic patients administered subcutaneously with 30 micrograms of pramlintide, three times a day for 14 days, was 70.6 $\pm$ 2.7. Thus, Applicants' allegation that Kolterman *et al.* (1996) says nothing about body weight or weight reduction in their patients is totally inaccurate. Clearly, the structural limitations or requirements of the instant claims are met by the teachings of Kolterman *et al.* (April, 1996). The very active step recited in the instantly claimed method was disclosed and practiced by Kolterman *et al.* in April, 1996. Thus, the prior art method is the *same* as the instantly claimed method in terms of the amylin agonist (pramlintide) administered, the diabetic patients used, the subcutaneous route of administration, and the dose and the daily frequency of the amylin agonist administered. Kolterman's (1996) method of subcutaneous administration of pramlintide to a diabetic patient necessarily serves as the instantly claimed method of treating obesity and therefore anticipates the instantly claimed method. As a matter of law Kolterman *et al.* (April, 1996) anticipates the instant invention. Irrespective of the mechanism(s) of action of the amylin agonist, pramlintide, and irrespective of whether amylin is a peripherally or centrally acting agent, whether or not pramlintide is an anorectogenic agent, gastric emptying-delaying agent, or a food intake-suppressing agent, the prior art method necessarily serves as Applicants' method of treating obesity as defined in the instant application, i.e., 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance'. See the art rejection set forth below.

(B) Kolterman *et al.* (WO 96/40,220)

Applicants submit the following arguments: (a) Kolterman *et al.* ('220) relates to methods of lowering blood sugar in patients with type 2 diabetes mellitus, who do *not* use insulin by

administration of an amylin agonist thereto. (b) It states that non-insulin-taking Type II diabetic patients may be treated by the administration of an amylin agonist in order to lower their blood glucose concentrations, one such agonist being $^{25, 28, 29}$pro-h-amylin. (c) Kolterman *et al.* ('220) do not refer to weight loss or treatment of obesity. (d) Dr. Kolterman is a named inventor on both instant application and the WO 96/40,220 cited by the Office, the latter being related to US patent 6,417,164 issued to Kolterman *et al.* on 9 July 2002 and US patent 6,143,718 issued to Kolterman *et al.* on 7 November 2000, both for treatment of type II diabetes mellitus with amylin agonists. (e) The parent application to the instant case was filed on 6 June 1997. One's own work is not prior art under § 102(a) even though it has been disclosed to the public in a manner or form which otherwise would fall under § 102(a). *In re Fout*, 213 USPQ 532 (CCPA 1982) and *In re Facius*, 161 USPQ 294, 302 (1969).

Applicants' arguments have been carefully considered, but are not persuasive. The rejection using the reference of Kolterman *et al.* (WO 96/40220, already of record) (Kolterman *et al.*, II) in view of Meglasson (US 5,134,164) has been withdrawn. A modified rejection has been set forth below wherein *et al.* (WO 96/40220) has been applied under 35 U.S.C § 102(a).

First, contrary to Applicants' assertion, there is no parent application to this case. Secondly, Kolterman *et al.* ('220) taught a method of administering to patients having type 2 diabetes mellitus, who took the usual dose of insulin. See paragraph bridging pages 22 and 23; and the first row in each Table of Kolterman *et al.* ('220) which explicitly recites "Insulin-treated patients". Applicants' argument that one's own work is not prior art under § 102(a) even though it has been disclosed to the public in a manner or form which otherwise would fall under § 102(a) is misplaced. First, despite the fact that Kolterman is a named inventor on both the instant application and the WO 96/40,220, the inventorship of the instant application (Duft and Kolterman) and the inventorship of WO 96/40,220 (Kolterman; Thompson; and Mullane) are non-identical. Therefore, the publication of Kolterman *et al.* ('220) is proper prior art under 35 U.S.C. § 102(a). The term "others" in 35 U.S.C. 102(a) refers to any entity which is different from the inventive entity. The entity need only differ by one person to be "by others." This holds true for all types of references eligible as prior art under 35 U.S.C. 102(a) including publications

as well as public knowledge and use. See MPEP 2132 III.

The very active step of the instantly claimed method was disclosed and practiced by Kolterman *et al.* ('220) in 1996 in the very same patient population used by Applicants in Example 1 of the instant application. Given Kolterman's ('220) express teaching that obesity is a characteristic of 'most patients with Type II diabetes mellitus', Kolterman's ('220) method of subcutaneous administration of pramlintide to a Type II diabetic patient in an amount that falls within the range recited in the instant claims necessarily serves as the claimed method of treating obesity and therefore anticipates the instantly claimed method. The prior art method is the *same* as the instantly claimed method in terms of the amylin agonist (pramlintide) administered, the insulin-taking Type II diabetic patient population used, the subcutaneous route of administration, the dose and the daily frequency of the amylin agonist administered, and the administration step prior to a meal. Since the structural limitations of the instant claims are clearly met by the teachings of Kolterman *et al.* ('220), Kolterman's ('220) method is expected to serve as the instantly claimed method and is expected to bring about the same therapeutic effect against the intrinsic obesity in said Type II diabetic patients. See the art rejection set forth below.

Scope of Instant Invention

32) The instant invention encompasses within its scope the following:

(a) The limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See last paragraph on page 9 of the substitute specification:

> ..... the management and care of a patient for the purpose of combating the disease, condition or disorder, and includes the administration of an amylin or an amylin agonist to prevent the **onset of symptoms or complications, alleviating the symptoms or complications**, or eliminating the disease condition or disorder. Treating or preventing obesity therefor includes the inhibition of weight gain and inducing weight loss in patients in need thereof. Additionally, treating or preventing obesity is meant to include **controlling weight for cosmetic purposes in humans**, that is **to control body weight to improve bodily appearance**. [Emphasis added].

(b) The limitation 'human subject' in the instant claims does not exclude 'a 70 kg patient'. In fact, the now recited amylin or amylin agonist 'amount' of 'about 0.01 mg to about 5

mg per day' is indeed 'for a *70 kg patient*, administered in a single, divided or continuous doses' [Emphasis added]. See first full paragraph on page 23 of the substitute specification. See also paragraph bridging pages 23 and 24; and lines 3-7 on page 24 of Applicants' response filed December 2002.

(c) The term 'human subject' broadly encompasses any human subject, including type I and type II diabetic patient. The human patient population used in Example 1 of the instant application is of Type II diabetes mellitus.

(d) It is noted that the method claimed in claims 1-5, 7, 8 and 14-16 does not require that a specific amount of the recited amylin or amylin agonist be administered. The method of claims 1-3, 7, 8, 13 and 14-16 does not require that the recited amylin or amylin agonist be administered via a specific route. Claims 1-4, 7, 9-14 and 16 encompass methods of administering the recited amylin or amylin agonist for a period of hours, days, weeks or months. Claims 1-3, 14 and 16 encompass administration of any amylin or amylin agonist by any route, in any quantity, and any number of times per day, to any human subject for any length of time.

(e) The substitute specification at paragraph bridging pages 7 and 8 characterizes 'increased appetite' as a sign strongly associated with obesity (see second paragraph). Thus, increased appetite and therefore, increased food intake is a 'symptom' of obesity and plays an important role in obesity. The description in the last paragraph on page 9 of the substitute specification states that the claimed method of treatment encompasses alleviating the 'symptoms' of the disorder, i.e., obesity.

Double Patenting

33) Claims 14 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 64 and 68 of US patent 6,956,026 ('026, filed 01/07/1997). Although the conflicting claims are not identical, they are not patentably distinct from each other. There is no indication in the instant specification of what is being excluded by the language 'active anti-obesity agent consisting *essentially* of an amylin or an amylin agonist'. Absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of', is construed as equivalent to 'comprising'. See e.g., *PPG*,

156 F.3d at 1355, 48 USPQ2d at 1355.

Beeley's ('026) method of *reducing body weight* comprising peripheral administration of a therapeutically effective amount of an amylin agonist falls within the scope of the instant claims and therefore anticipates the instant claims. The portion of the '026 disclosure providing support for a subject being administered with an amylin agonist includes a human subject having the obesity disorder (see paragraphs 2 and 3 in column 4).

34) Claims 7, 14 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 85 of the U.S. patent 5,739,106 (Rink *et al.*). Although the conflicting claims are not identical, they are not patentably distinct from each other. The open claim language 'comprising' in claims 7 and 14 includes any other element other than amylin agonist in the recited composition. There is no indication in the instant specification of what is being excluded by the language in claim 16 'composition consisting *essentially* of an amylin or an amylin agonist'. Absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of', is construed as equivalent to 'comprising'. See e.g., *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355.

It is noted that 'the inhibition of weight gain' is not excluded from the scope of the claimed method, but is expressly encompassed. See lines 14 and 5 of page 9 of the substitute specification.

The method claimed in claim 85 of the '106 patent for *control of body weight* in a mammal comprising administering to said mammal a composition comprising the amylin agonist, $^{25, 28, 29}$pro-h-amylin, falls within the scope of the instantly claimed method. The portion of the '106 disclosure providing support for a 'mammal' expressly includes a human subject and the disclosure providing support for 'control of body weight' includes control of body weight resulting from controlled appetite, less food being taken in per meal, a longer tome elapsing between meals, and suppression of food intake. See second full paragraph in column 7.

35) Claims 7, 13, 14 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract). Although

the conflicting claims are not identical, they are not patentably distinct from each other. There is no indication in the instant specification of what is being excluded by the language 'active anti-obesity agent consisting *essentially* of an amylin or an amylin agonist' [Emphasis added]. Absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of', is construed as equivalent to 'comprising'. See e.g., *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355.

The method claimed in claims 34 and 35 of the US patent 5,686,411 is for the treatment of diabetes mellitus in a mammal comprising the administration to said mammal of a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin. The portion of the disclosure of the '411 patent at lines 45-53 in column 7 supporting the limitation mammal does not exclude, but expressly includes a patient seen by a medical practitioner, i.e., a human. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg of the agonist. The amount recited in claim 13 falls within this range. The portion of the disclosure of the U.S. patent '411 at lines 9-12 of column 3 that describes the limitation 'diabetes mellitus' includes insulin-requiring diabetes mellitus. Given the art-known fact that up to 90% of diabetic patients are intrinsically obese as disclosed by Tsanev, the method of the '411 patent comprising the step of administration of a therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to a diabetic human, anticipates the instant claims. Given that the method steps of the '411 patent and the instant claims are the same, the method of the '411 patent is expected to bring about a therapeutic effect against intrinsically obese diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients.

36) Claims 7, 13, 14 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract) and Rink *et al.* (US 5,739,106) ('106). Although the conflicting claims are not identical, they are not patentably distinct from each other. There is no indication in the instant specification of what is being excluded by the language 'active anti-obesity agent consisting *essentially* of an amylin or an

amylin agonist' [Emphasis added]. Absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of', is construed as equivalent to 'comprising'. See e.g., *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355.

The method claimed in claims 11 and 13 of the US patent 5,321,008 is for the treatment of diabetes mellitus in an insulin-requiring mammal comprising the administration to said mammal of a therapeutically effective amount of a calcitonin alone, or calicitonin and insulin. The portion of the disclosure of the '008 patent at first full paragraph in column 13 supporting the limitation 'therapeutically effective amount' includes the typical dosage units of about 0.1 to 1 mg of calcitonin. Given the art-known fact that calcitonin is an amylin agonist as taught at line 4 of column 16 of Rink *et al.* ('106) and the art-known fact that up to 90% of diabetic patients are intrinsically obese as disclosed by Tsanev, the method of the '008 patent comprising the step of administration of a therapeutically effective amount of calcitonin to a type 2 diabetic human anticipates the instant claims. Given that the method steps of the '008 patent and the instant claims are the same, the method of the '008 patent is expected to bring about a therapeutic effect against the intrinsic obesity in the type 2 diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients.

37) Claims 7, 13, 14 and 16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 33 of the co-pending application 09/445,517. Although the conflicting claims are not identical, they are not patentably distinct from each other. There is no indication in the instant specification of what is being excluded by the language 'active anti-obesity agent consisting *essentially* of an amylin or an amylin agonist'. Absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of', is construed as equivalent to 'comprising'. See e.g., *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355.

The method claimed in claim 33 of the co-pending application, 09/445,517 of *treating obesity* in a human subject comprising administering a composition comprising an anti-obesity agent consisting essentially of amylin or an amylin agonist as recited therein falls within the scope of the instant generic claims and therefore anticipates the instant claims.

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

38) Claims 7, 14 and 16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of the co-pending application, 10/851,574.

It is noted that the assignee of the pending application 10/851,574 is Amylin Pharmaceuticals Inc.

Although the conflicting claims are not identical, they are not patentably distinct from each other. There is no indication in the instant specification of what is being excluded by the language 'active anti-obesity agent consisting *essentially* of an amylin or an amylin agonist'. Absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of', is construed as equivalent to 'comprising'. See e.g., *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355.

The method claimed in claim 6 of the co-pending application, 10/851,574 of *reducing body fat gain* in an overweight or obese human subject comprising administering to the human subject an amylin or amylin agonist falls within the scope of the instant claims and therefore anticipates the instant claims. The portion of the disclosure of the co-pending application, 10/851,574 that provides support for the amount or dose of amylin or amylin agonist does not exclude, but expressly includes an amount in the range of from about 1 to 300 micrograms to about 5 mg/day (see paragraph above Example 1).

This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

39) Claims 8-13 rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 8-13 include the limitation: "anti-obesity agent". However, there is no descriptive

support in the instant specification for this limitation. See paragraph 28 *supra*. Therefore, the new limitation in the new claims is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

40) Claim 14 is rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 14 includes the limitation: 'amylins' and 'pharmaceutically acceptable' salts thereof. However, there is no descriptive support in the instant specification for these new limitations. Therefore, the above-identified limitation in the new claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

41) Claim 15 is rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 15 includes the limitation: 'weight of said human subject is lower following four weeks of treatment'. However, there appears to be no descriptive support in the instant specification for these new limitations. Therefore, the above-identified limitation in the new claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

42) Claim 8 is rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 8 includes the limitation: 'at least about' four weeks. The terms 'at least' and 'about' with regard to the limitation 'four weeks' lack descriptive support. However, there appears to be no descriptive support in the instant specification for these new limitations. The term 'at least' has no upper limit and includes any number above four. Therefore, the above-identified limitation in the new claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

43) Claim 1 and those dependent therefrom and claim 16 are rejected under 35 U.S.C § 112,

first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1 and 16 include the limitation: 'an effective amount of a composition'. However, there appears to be no descriptive support in the instant specification for these new limitations. The original claim 1 included the limitation: 'an effective amount of an amylin or an amylin agonist', but not 'an effective amount of a composition'. Therefore, the above-identified limitation in the new claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c).

Applicants are invited to point to the descriptive support in specific pages and lines of the disclosure, as originally filed, for the limitation identified above, or remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

44) Claims 2-16 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 7 and 16 vague and indefinite in the recitation: "an effective amount of a composition" (see line 2), because the limitation "effective" is a relative term which renders the claim indefinite. The limitation "effective" is not specifically defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of effectiveness, and one of ordinary skill in the art would not be able to reasonably envisage the scope of the invention. Whether or not the recited 'amount' encompasses therapeutically effective amount, prophylactically effective amount, pharmacologically effective amount or immunologically effective amount, is not understood. See paragraph 29 above.

(b) Claims 2-6 and 9-13 lack proper antecedent basis in the limitation: 'A method according to claim ...'. For proper antecedence and consistency with claims 8 and 15, it is suggested that Applicants replace the limitation with --The method according to claim ....--.

(c) Claim 3 is confusing in the use of brackets while reciting '[SEQ ID NO: 1]. It is unclear whether the brackets are intended to delete the limitation 'SEQ ID NO: 1', or are intended to appear in the printed patent. If the latter is intended, it is suggested that Applicants replace the limitation with the limitation --(SEQ ID NO: 10)--.

(d) Claim 15 is vague and indefinite in the limitation: 'lower'. The term 'lower' is a relative term which renders the claim indefinite. The term 'lower' is not specifically defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

(e) Claims 9-13 are vague, indefinite and confusing in the limitations: 'an effective amount of an anti-obesity agent .... is administered ... in an amount of'. These claims depend from claim 1, which includes the limitation: 'an effective amount of a composition comprising an anti-obesity agent'. It is unclear whether the recited 'effective amount' is pertinent to the recited 'composition' or the 'anti-obesity agent'?

(f) Claims 3, 5, 6, 8-10 and 15, which depend directly or indirectly from claim 4 or 4, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

45) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

46) Claims 7, 14 and 16 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Beeley *et al.* (US 6,956,026).

It is noted that the transitional recitation 'comprising' is open-ended claim language and

therefore does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1].

The use of the limitation 'consisting *essentially* of an amylin or amylin agonist' in claim 16 has been noted. MPEP § 2111.03 states that claims recited in 'consisting essentially of' language should be construed as if recited in open 'comprising' language, absent some evidence that the additional ingredients in the prior art process/product materially affect the basic and novel characteristics of the claimed invention. There is no indication in the instant specification of what is being excluded by the language 'active anti-obesity agent consisting *essentially* of an amylin or an amylin agonist'. Absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of' will be construed as equivalent to 'comprising'. See e.g., *PPG*, 156 F.3d at 1355, 48 USPQ2d at 1355.

Beeley *et al.* ('026) taught a method of treating conditions or disorders which can be alleviated by reducing food intake, or a condition or disorder in which the reduction of food intake is of value, including *obesity*, or type II diabetes, comprising administration of an effective amount of a composition comprising a compound that affects satiety, such as, an amylin agonist. The subject is human. Beeley's ('026) method is useful for reducing the appetite and reducing the weight of the subjects (see 'Field of the Invention'). See also claims, particularly claims 1, 3, 10, 16, 19, 26, 32, 33, 35, 42, 46, 47, 49, 56, 60, 61, 63, 64, 65, 67 and 68. The method involves the administration of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and one or more of a compound that exhibits a long term or short-term satiety action, such as, amylin, an amylin agonist, for example, pramlintide or AC-137 or ^{25,28,29}Pro-human amylin. The composition is a *single* composition comprising amylin or amylin agonist, and the composition is advantageously administered separately from extendin or extendin agonist (see first, third and fourth full paragraphs in column 5; and third full paragraph in column 13). Thus, the prior art composition that comprises one amylin agonist compound exhibiting a long term or short-term satiety action, such as, pramlintide, does not contain cholecystokinin or cholecystokinin agonist, or consists essentially of the amylin agonist. The prior art method that comprises the separate administration of a single amylin or amylin agonist composition meets the active administration step of the instantly claimed method. The pharmaceutical composition is administered subcutaneously (see lines 34-37 in column 14). Beeley *et al.* further taught that a suitable

administration format may be best determined by a medical practitioner for each patient individually as described in standard formulation treatises, e.g., *Remington's Pharmaceutical Sciences* by EW Martin (see lines 32-42 in column 13). The typical effective daily dose of the compound is in the range of 10 micrograms to 5 mg per day, or about 30 to about 500 micrograms to 5 mg per day, administered in a single or divided doses (i.e., more than one doses per day). Beeley *et al.* further taught that the exact dose to be administered is determined by the attending clinician and is dependent upon where the particular compound lies within the above-quoted range, as well upon the age, weight and condition of the individual. Beeley *et al.* taught that administration should begin whenever the suppression of food intake, or weight lowering is desired, for example, at the first sign of symptoms or shortly after diagnosis of *obesity*, diabetes mellitus, or insulin resistance syndrome. See paragraph bridging columns 14 and 15.

The required active step of the instantly claimed method is clearly met by the prior art method in that pramlintide is subcutaneously administered to a human subject in whom weight lowering is desired. The structural limitations of the claimed method are met by the disclosure of Beeley *et al.*, and therefore the instant claims are anticipated by Beeley *et al.*

47) Claims 1-9 and 11-16 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996, already of record) (Kolterman *et al.*, 1996).

It is noted that the 'human subject' recited in the instant claims encompasses both insulin-taking and non-insulin-taking human subject. It is further noted that a 70 kg patient is not excluded from the scope of the instant invention, but is expressly included. For example, the recited amount range of 'about 0.01 to about 5 mg/day' of amylin agonist, for example, pramlintide to be administered, is specifically "for a 70 kg patient". See first full paragraph on page 23 of the substitute specification.

It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See second paragraph on page 9 of the substitute specification.

Kolterman *et al.* (1996) taught a method of subcutaneous administration of 30, 100 or 300 μg of pramlintide or AC137 (i.e., $^{25, 28, 29}$pro-h-amylin), a human amylin analogue, to human patients with insulin-dependent diabetes mellitus or IDDM who are on insulin. Pramlintide is administered three times daily for a period of 14 days (see abstract; and page 493). Kolterman's pramlintide composition did not comprise cholecytokinin or cholecystokinin agonist, but consisted essentially of pramlintide. Thirty micrograms three times a day amount to 'about 0.1 milligrams' per day. Kolterman's (1996) patients who were treated with 30 micrograms of subcutaneously administered pramlintide showed a lower body weight of 70.6 ± 2.7 kg compared the placebo controls whose body weight was about 4.0 kg higher, i.e., 74.5 ± 2.7 kg (see Table 1). It should be noted that a 70 kg patient is not excluded from the scope of the instant invention, but is expressly included. For example, the recited amount range of 'about 0.01 to about 5 mg/day' of amylin agonist, for example, pramlintide, is specifically "for a 70 kg patient". See first full paragraph on page 23 of the substitute specification; and paragraph bridging pages 23 and 24, and first full paragraph on page 24 of Applicants' response filed December 2002. This is important because the mean body weight $\pm$ SEM of Kolterman's (1996) diabetic placebo population was 74.5 ± 2.4 kg, whereas the mean body weight of the 15 diabetic patients administered subcutaneously with 30 micrograms of pramlintide, three times a day for 14 days, was 70.6 ± 2.7. Thus, Kolterman's (1996) method did reduce or lower the body weight of the human diabetic subjects administered 30 micrograms of pramlintide, and therefore, improved the bodily appearance of the treated patients, and thus necessarily served as a method of treating obesity as defined in the instant application.

Irrespective of the mechanism(s) of action of the amylin agonist pramlintide and irrespective of whether amylin is a peripherally or centrally acting agent, whether or not pramlintide is an anorectogenic agent, gastric emptying-delaying agent, or a food intake suppressing agent, the prior art method necessarily serves as Applicants' method of treating obesity as defined in the instant application, i.e., 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance'.

Claims 1-9 and 11-16 are anticipated by Kolterman *et al.* (1996).

48) Claims 1-7, 9-14 and 16 are rejected under 35 U.S.C § 102(a) as being anticipated by

Kolterman *et al.* (WO 96/40220, already of record) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract).

It is noted that the inventorship of the Kolterman ('220) publication (Kolterman, Thompson, and Mullane) is non-identical with the inventorship of the instant application (Duft and Kolterman). Therefore, the publication of Kolterman *et al.* ('220) is proper prior art under 35 U.S.C. § 102(a). See MPEP 2132 III.

It is noted that the 'human subject' recited in the instant claims encompasses both insulin-taking and non-insulin-taking human subject. It is further noted that a 70 kg patient is not excluded from the scope of the instant invention, but is expressly included. For example, the recited amount range of 'about 0.01 to about 5 mg/day' of amylin agonist, for example, pramlintide to be administered, is specifically "for a 70 kg patient". See first full paragraph on page 23 of the substitute specification.

It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See second paragraph on page 9 of the substitute specification.

It is noted that the patient population used in the instant invention to treat obesity by the administration of the recited amount of pramlintide is insulin-requiring Type 2 diabetics. See Example 1 of the instant specification.

Kolterman *et al.* ('220) taught a method of administering to an insulin-taking type II diabetic subject a composition comprising a dose of 10, 30, 50, 60 or 150 micrograms per day (i.e., the amount falling in the range recited in the instant claims) of the amylin agonist, pramlintide or $^{25, 28, 29}$pro-h-amylin, also known as AC137. The composition consists of pramlintide and is administered in single or multiple doses, for example, TID, and/or QID times per day, in a dose of about 30 micrograms QID or about 60 micrograms TID or QID. See pages 9-11; paragraph bridging pages 20 and 21; page 21; first paragraph in page 19; and first row reciting 'Insulin-Treated Patients' in each Table. Pramlintide is administered subcutaneously 1-4 times a day before meals (see pages 9 and 22). The composition comprises a pharmaceutically

acceptable carrier (see lines 8-10 on page 19). Kolterman *et al.* ('220) additionally taught that the presence of obesity is a characteristic of 'most patients with Type II diabetes mellitus' (see page 10). Thus, the very active step of the instantly claimed method was disclosed and practiced by Kolterman *et al.* ('220) in 1996 in the very same patient population used by Applicants in Example 1 of the instant application. Given Kolterman's ('220) express teaching that obesity is a characteristic of 'most patients with Type II diabetes mellitus', Kolterman's ('220) method of subcutaneous administration of pramlintide to a Type II diabetic patient in an amount that falls within the range recited in the instant claims necessarily serves as the claimed method of treating obesity and therefore anticipates the instantly claimed method. The prior art method is the *same* as the instantly claimed method in terms of the amylin agonist (pramlintide) administered, the insulin-taking Type II diabetic patient population used, the subcutaneous route of administration, the dose and the daily frequency of the amylin agonist administered, and the administration step prior to meals. Since the e structural limitations of the instant claims are clearly met by the teachings of Kolterman *et al.* ('220), Kolterman's ('220) method is expected to serve as the instantly claimed method and is expected to bring about the same therapeutic effect.

The Office's position that Kolterman's ('220) method is the same as the Applicants' claimed method is based upon the fact that the method step, the compound administered, the amount of the compound administered, and the route by which the compound is administered, and the human patient population to which the compound is administered, are overlapping in the two methods. There is sufficient overlap between the prior art method and the Applicants' method to reasonably conclude that Kolterman's ('220) method is one and the same as the Applicants' method. Given the art-known fact that up to 90% of diabetic patients are intrinsically obese as disclosed by Tsanev, Kolterman's ('220) method comprising the step of administration of a therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to a type 2 diabetic human anticipates the instant claims. Given that the method step of the Kolterman's ('220) method and the instant claims is the same, Kolterman's ('220) method is expected to bring about a therapeutic effect against the intrinsic obesity in the type II diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients. Since the Office does not have the facilities for examining

and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed product and the product of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald et al.*, 205 USPQ 594. MPEP 2112 refers to *In Re Best* to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the claimed method, any assertions of specific functional properties attributed to the amylin or amylin agonist in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 1-7, 9-14 and 16 are anticipated by Kolterman *et al.* ('220).

Relevant Art

49) The art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- Szabo *et al.* (*Vnitr Lek* 44: 145-150, March 1998) taught that up to 90% of type II diabetic (NIDDM) patients are obese (see abstract).
- Mack *et al.* (US 20050197287 A1) expressly disclose that in humans, 'patients who are overweight or obese are considered those with a Body Mass Index or BMI of equal to or greater than 25'. See lines 1-3 in section [0004]. Mack *et al.* teach that according to the NIH Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults, all adults who have a 'BMI of 25 or more' are considered at risk for premature death and disability as a consequence of overweight and obesity. See section [0005].
- Arnelo *et al.* (*Am. J. Physiol.* 271: R1654-R1659, 1996, already of record) taught the anorectic effect of IAPP in rats. Arnelo *et al.* taught that *subcutaneously* administered IAPP dose-dependently inhibited food intake and decreased body weight gain. Arnelo *et al.* taught that IAPP may play an important physiological or pathophysiological role in control of food intake (see abstract).

Arnelo *et al.* (*Scand. J. Gastroenterol.* 31: 83-89, 1996, already of record) showed that chronic increase of circulating IAPP levels can cause a marked reduction in both food intake

and body weight in rats (see abstract).

- Morley *et al.* (*Peptides* 12: 865-869, 1991, already of record) showed that amylin decreased food intake both in diabetic and non-diabetic mice (see abstract; and Figures 1 and 2).

- Andrew Young *et al.* (*Nutrition* 14: 524-527, 1998, already of record) must be noted [Emphasis added]:

> Several groups have reported an effect of amylin to inhibit food intake.[28-30] This effect is as potent as that of cholecystokinin (CCK), the prototypic peripheral satiety agent ...
> ... amylin, via its hormonal actions, may be relevant to the treatment of both forms of diabetes, ... potently inhibits gastric emptying. .... Of peptides known to be secreted in response to ingested carbohydrate, only amylin .... reported to inhibit gastric emptying at near-physiologic concentrations,[19]
>
> Amylin reduces food intake in rodents. This action, which synergizes with a similar action of CCK, could reflect a role as short-term peripheral satiety agent. Amylin **alone** or in combination with CCK may be useful in moderating caloric intake in **obesity** and other metabolic disorders.
>
> In different studies, pramlintide has been shown to slow gastric emptying in man[17].
>
> Amylin is the most potent mammalian inhibitor of gastric emptying identified thus far[19]. ... amylin is a physiologic regulator of gastric emptying.

- A.A. Young *et al.* (*Nutrition* 45: 1-3, January 1996) taught the dose-dependent slowing of gastric emptying by *subcutaneously* administered amylin or cholecystokinin in a rodent model (see pages 1-2 and Figure 1). A.A. Young *et al.* taught that amylin is the most potent inhibitor of gastric emptying (see page 3).

- Claim 3 of US 5,175,145 issued to Garth Cooper of Amylin Pharmaceuticals identified CGRP is an amylin agonist that has amylin activity as opposed to an amylin antagonist.

- EP 0 408 294 A2 refers to CGRP 8-37 as 'the amylin agonist CGRP 8-37' (see line 38 on page 8).

- Scherbaum WA (*Exp. Clin. Endocrinol. Diabetes 106*: 97-102, 1998) taught that people with both type 1 *and* type 2 diabetes are 'amylin deficient' (see first full paragraph in left column on page 99).

- Despite the existence of the US patents 5,280,014 and 5,364,841, Rink *et al.* (US 5,739,106) used an amylin agonist such as $^{25, 28, 29}$pro-h-amylin in a method for *control of body weight* in a mammal including a human (see claim 85 and second full paragraph in column 7). Rink *et al.* expressly acknowledged the previously known biologic properties of amylin such as food intake-reducing and anorectic effects (see paragraph bridging columns 6 and 7). Rink *et al.* expressly taught that an amylin agonist-containing therapeutic composition is useful in the

claimed methods of controlling appetite and/or *control of body weight* (see third full paragraph in column 7). An amylin agonist is defined herein as a compound having 'one' or more of the known biological activities of amylin, in particular the 'ability to reduce food intake'.

- Well before the filing date of the instant application, well before the effective filing date of the US patent 5,739,106, and well before the issuance of US patents 5,280,014 and US 5,364,841, Balasubramaniam *et al.* (WO 94/26292) disclosed several amylin analogs that behave as amylin agonists and exhibit an appetite suppressant effect. Balasubramaniam *et al.* taught that amylin serves as an *anorectic agent* (see lines 8 and 9 of page 3), while amylin antagonists *increase* appetite (see abstract; and last paragraph on page 21). Most importantly, Balasubramaniam *et al.* expressly taught in 1994 that '**amylin agonists are useful for treating problems of overweight**'. Balasubramaniam *et al.* expressly suggested the administration of amylin agonists to a *human* by one of the traditional modes, including parenteral mode, for the **treatment of obesity** (see lines 11 and 12 on page 9; last paragraph on pages 21 and 22) [Emphasis added]. Balasubramaniam *et al.* further taught a method of controlling food intake in a human comprising administering to said human a therapeutic amount of an amylin analog (see claim 13). Clearly, Balasubramaniam *et al.* suggested amylin agonists as anti-obesity agents in 1994.

- Kosmiski *et al.* (*Curr. Opin. Endocrin. Diabet.* 4: 36-39, 1997) reviewed the impact of appetite suppressant therapy on both weight loss and metabolic parameters in patients with NIDDM (see abstract). Kosmiski *et al.* taught that 'the majority of patients with NIDDM are obese' and that 'reduction of body weight is therapeutic in obese patients with NIDDM'. Kosmiski *et al.* taught that '[n]umerous studies have indeed shown that appetite suppressants reduce body weight in obese NIDDM patients' (see page 36).

Remarks

50) Claims 1-16 stand rejected.

51) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted to the PTO Central Fax number (571) 273-8300 which receives transmissions 24 hours a day and 7 days a week.

52) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

53) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

May, 2006

S. DEVI, PH.D.
PRIMARY EXAMINER